

IMPLICATIONS OF THE LATEST DORSAL COCHLEAR NUCLEUS MODEL FOR BLAST INJURY TINNITUS

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The 2 most common causes of tinnitus are:

1. Hearing Loss
2. Muscle, tendon, joint (“SOMATIC”) disorders of the head and neck

From a BLAST Exposure

There can be

- Hearing Loss

 - Outer and Inner Hair cells

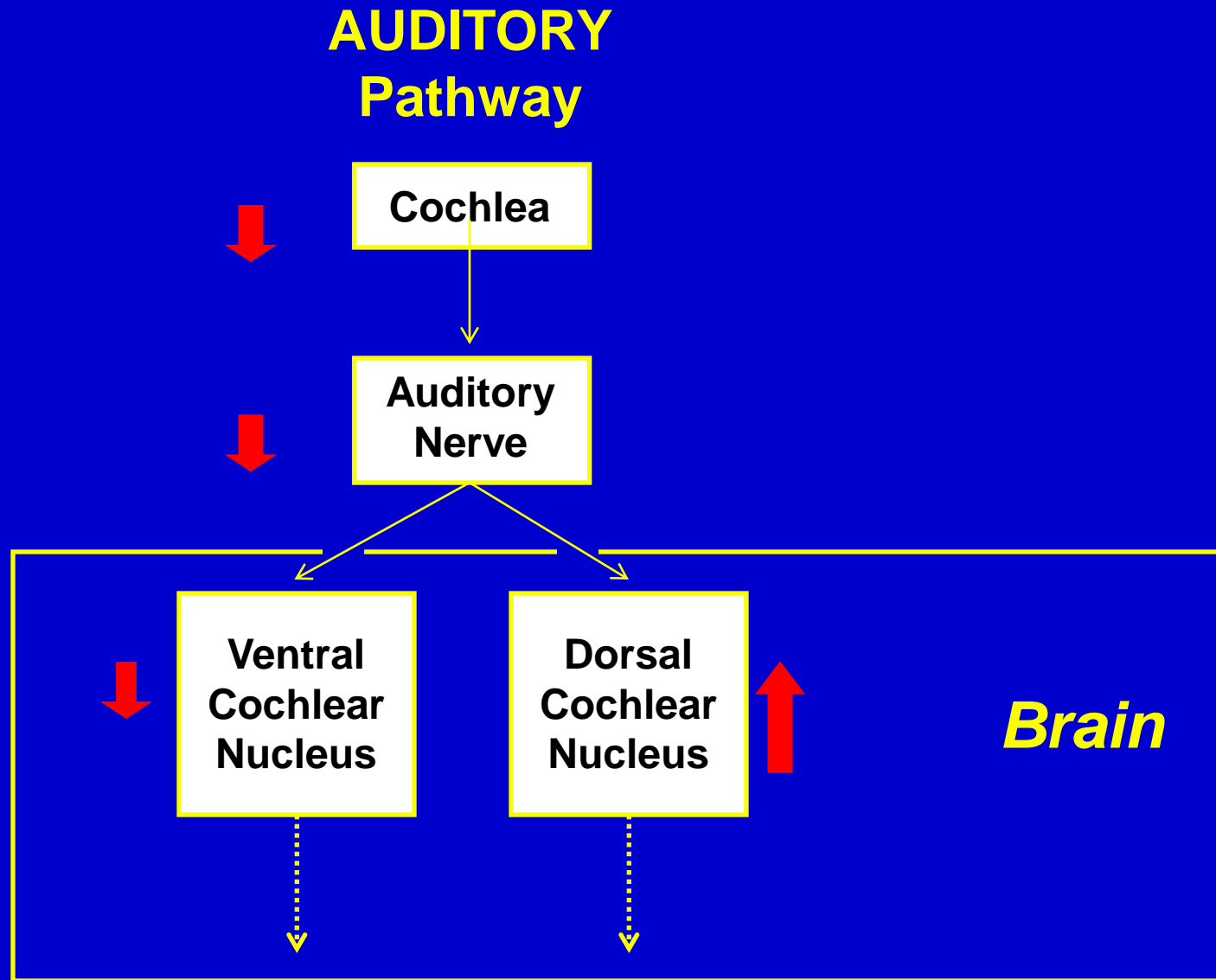
 - Type I and Type II Nerve Fibers

 - Efferents

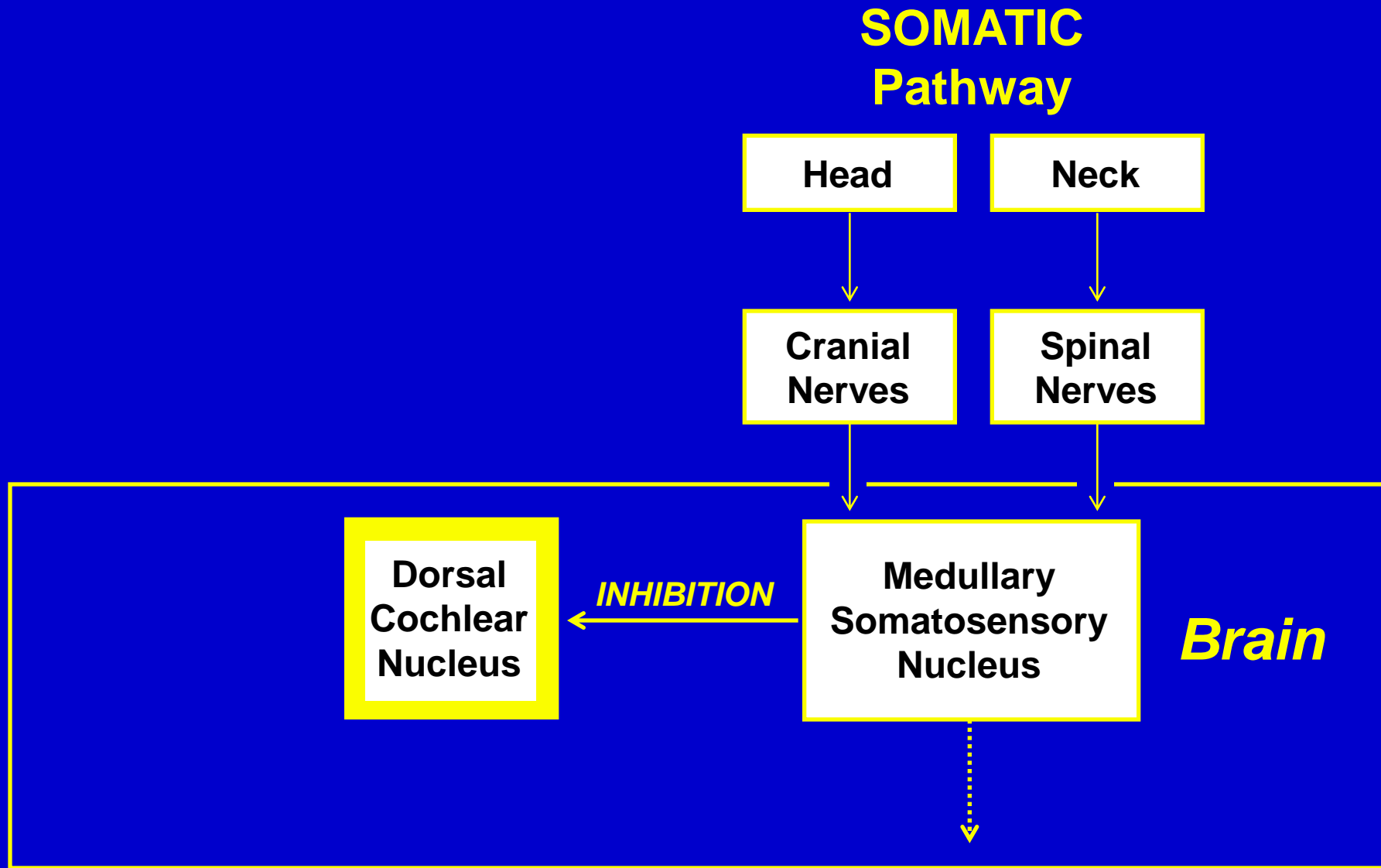
- Injuries to the head and neck

 - Muscle, tendon, joint (“SOMATIC”) disorders
of the head and neck

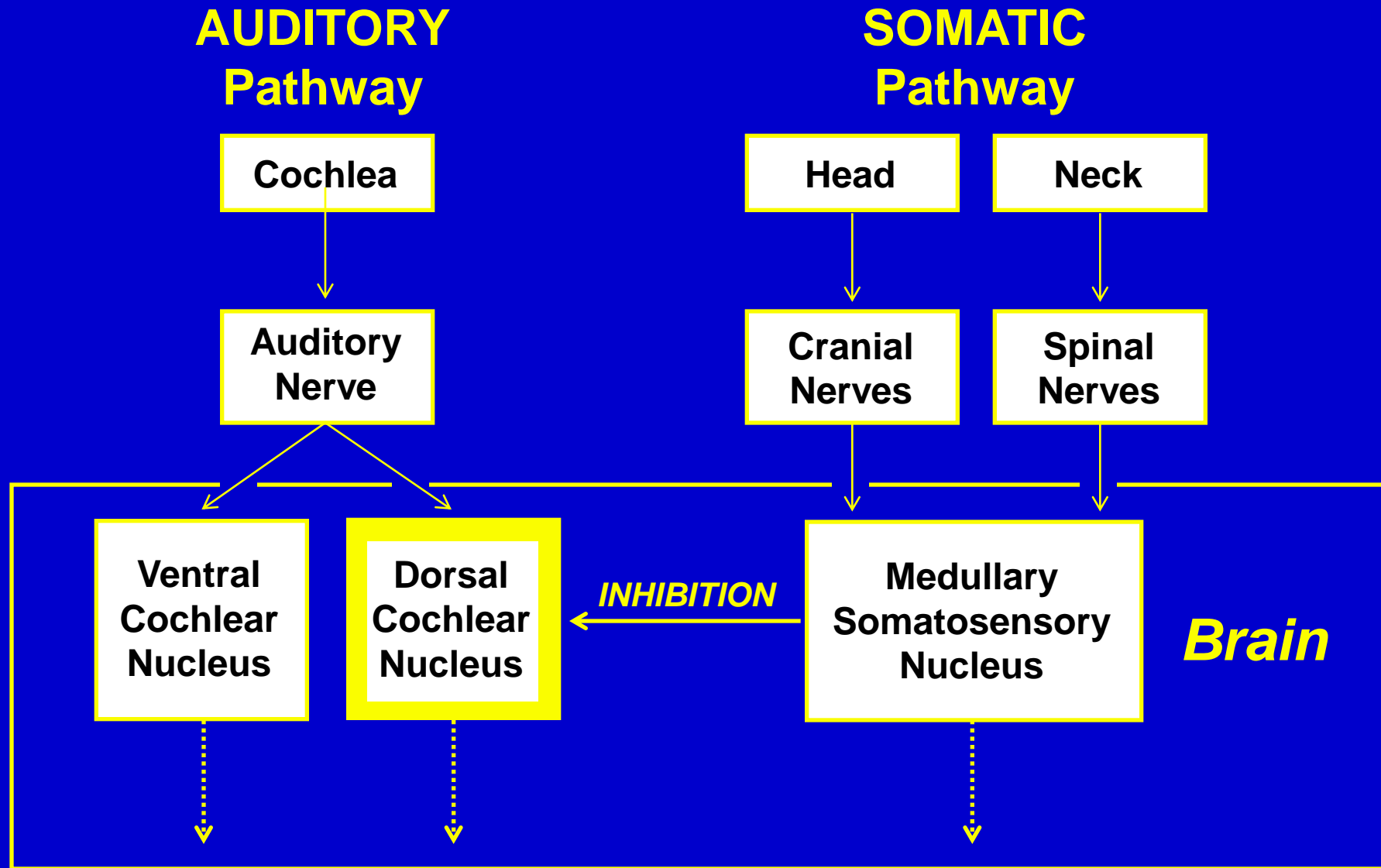
How UNILATERAL hearing loss causes UNILATERAL tinnitus



How SOMATIC disorders cause tinnitus



How hearing loss & SOMATIC disorders cause tinnitus



Levine, RA. (1999) Somatic (craniocervical) tinnitus and the dorsal cochlear nucleus (DCN) hypothesis

CASE STUDY

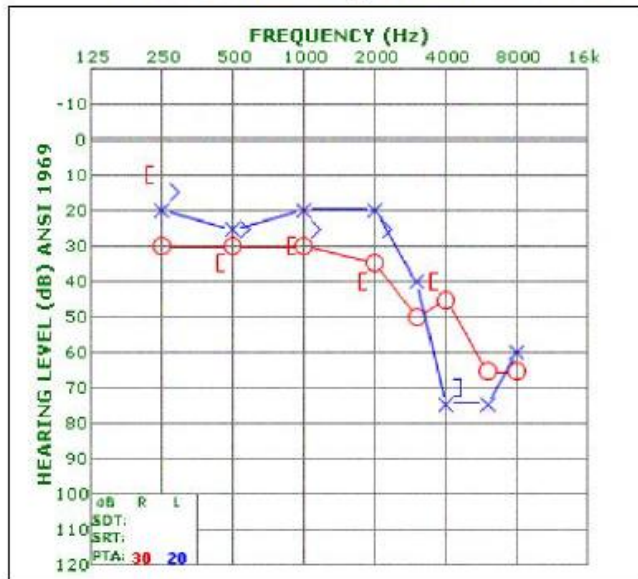
56 yo man with RIGHT ear tinnitus from an electric shock

The shock entered through his right hand

elicited immediate right tinnitus (no other hearing symptoms)
and chest pains

Audiogram

7 weeks following tinnitus onset



STANDARD somatic testing (only maneuvers that modulated his tinnitus are shown)

Condition	Right Side Tinnitus	Left Side Tinnitus
Baseline (0 - 10 Scale)	6	0
Open Jaw	6.5	0
against resistance	7	0
Protrude Jaw	8	0
LEFT Jaw deviation	7	0
Self-wiggling of right ear	6.5	0
RIGHT temple testing	10	0
RIGHT SCM	10	0

56 yo man with right ear tinnitus from an electric shock

Testing the sensitive right temporal region with other somatosensory modalities

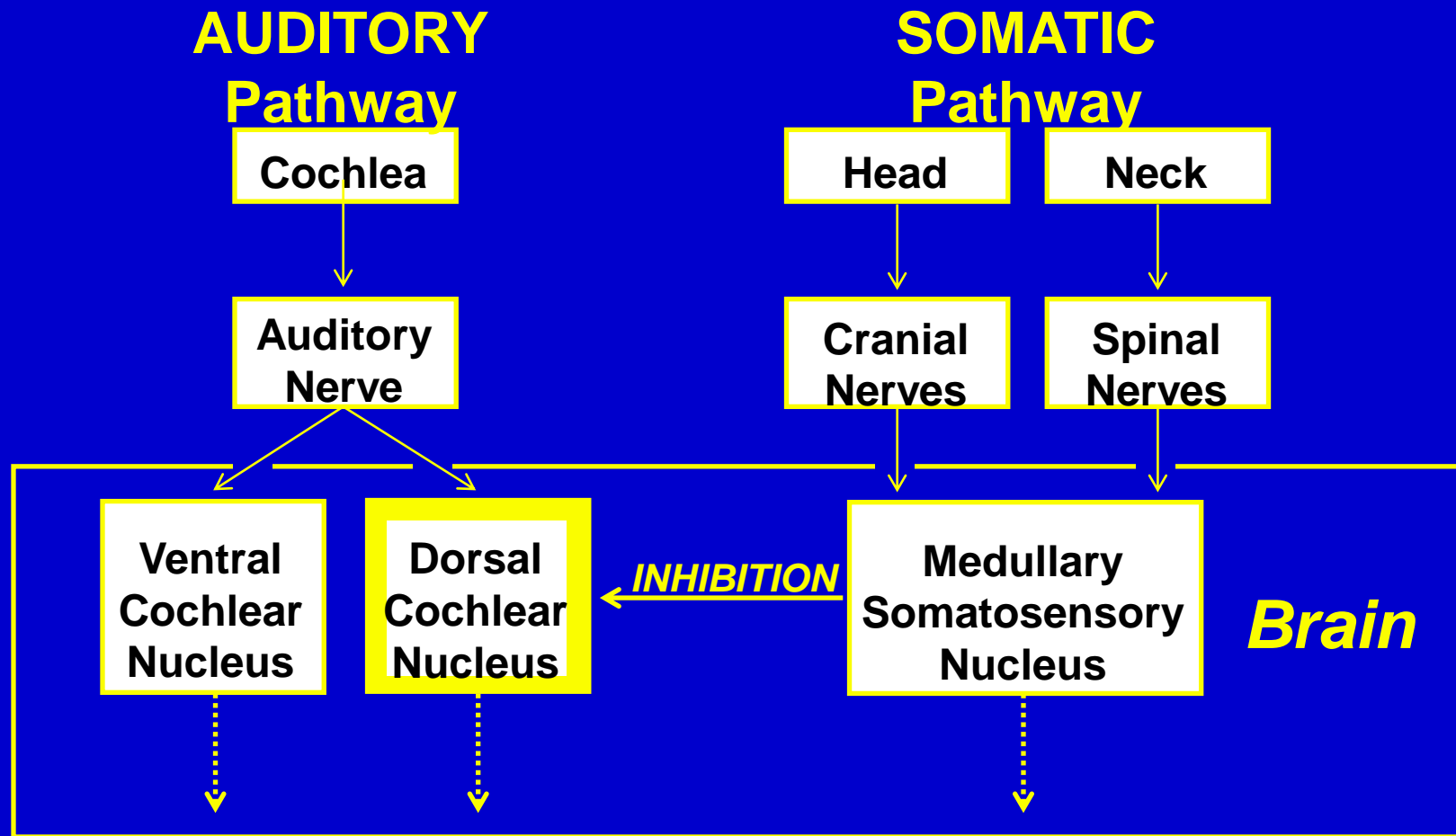
Modality	Sensory System	Right Side Tinnitus	Left Side Tinnitus
Baseline (0 - 10 Scale)		6	0
Light touch		No Change	0
Pulling overlying hair		No Change	0
Stretching overlying skin		No Change	0
Cooling	pain and temperature	No Change	0
Pin Prick	pain and temperature	No Change	0
Vibration	discriminative touch	10	0
Strong Pressure	discriminative touch	10	0



Somatosensory-auditory neural interactions within the central nervous system can account for many cases of tinnitus

CONCLUSION I:

IN ASSESSING TINNITUS FOLLOWING BLAST INJURIES, IN ADDITION TO HEARING LOSS, **SOMATIC DISORDERS OF THE HEAD AND NECK** MUST BE CONSIDERED IN DEVELOPING A COMPREHENSIVE AND EFFECTIVE TREATMENT PROGRAM



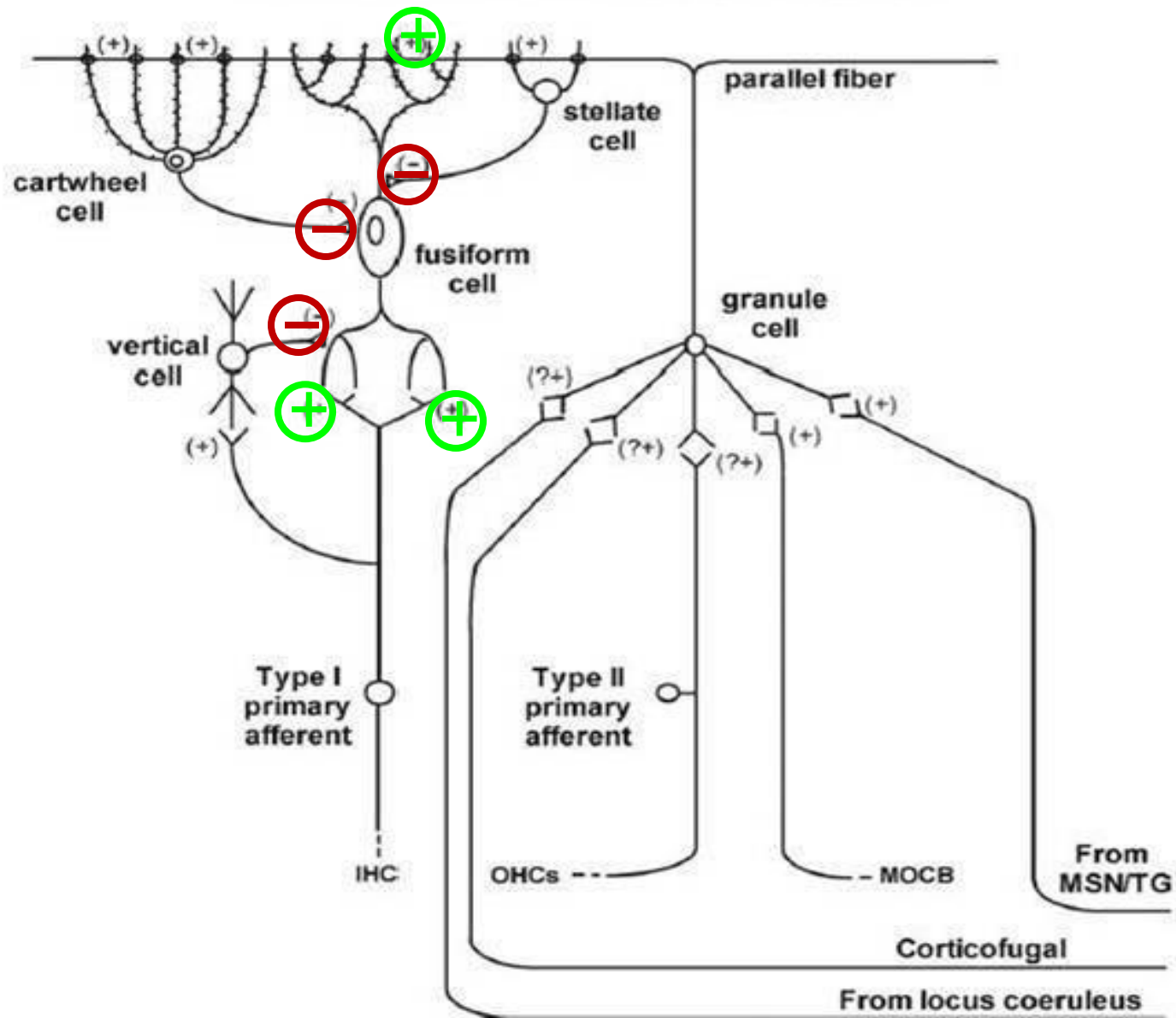
This simple block diagram cannot account for many puzzling properties of tinnitus – such as

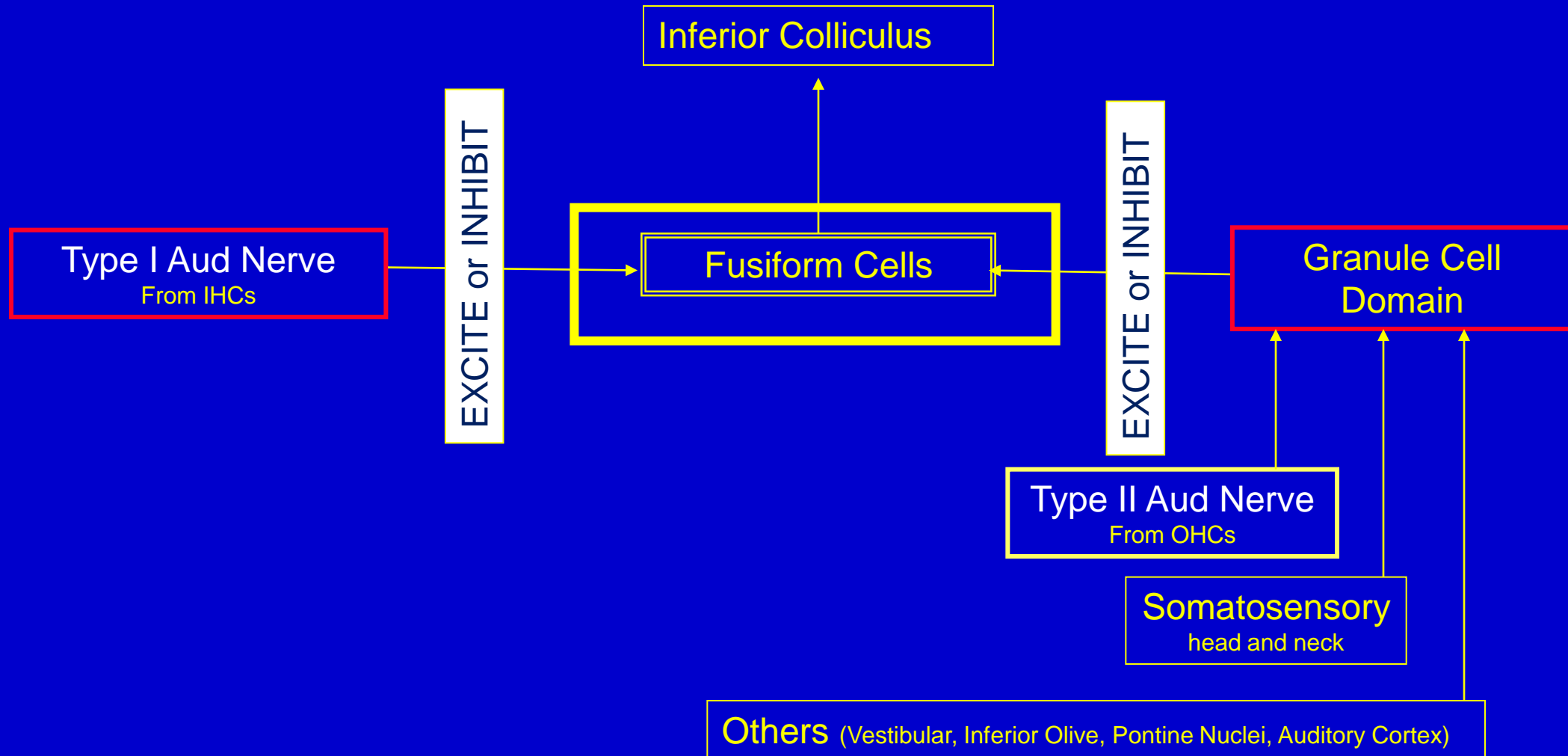
1. Why (a) hearing loss and (b) muscle problems of the head and neck can cause tinnitus in SOME PEOPLE BUT NOT OTHERS
2. Why total hearing loss causes tinnitus in SOME PEOPLE BUT NOT OTHERS
3. Why cutting the hearing nerve abolishes the tinnitus in SOME PEOPLE BUT NOT OTHERS
4. Why medications (~75%) quiet tinnitus in SOME PEOPLE BUT NOT OTHERS

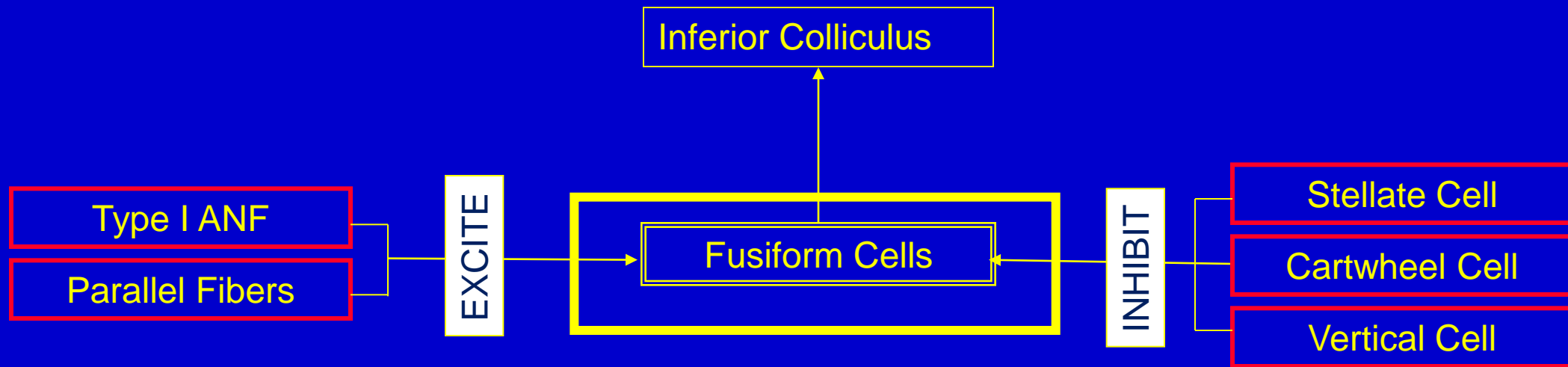
Our most recent modification to the DCN model for tinnitus includes more of the complexities of the DCN.

The fusiform cell is the main neural output of the DCN.

Our updated model incorporates the interplay of excitation and inhibition upon the fusiform cell from both auditory and non-auditory neural inputs.





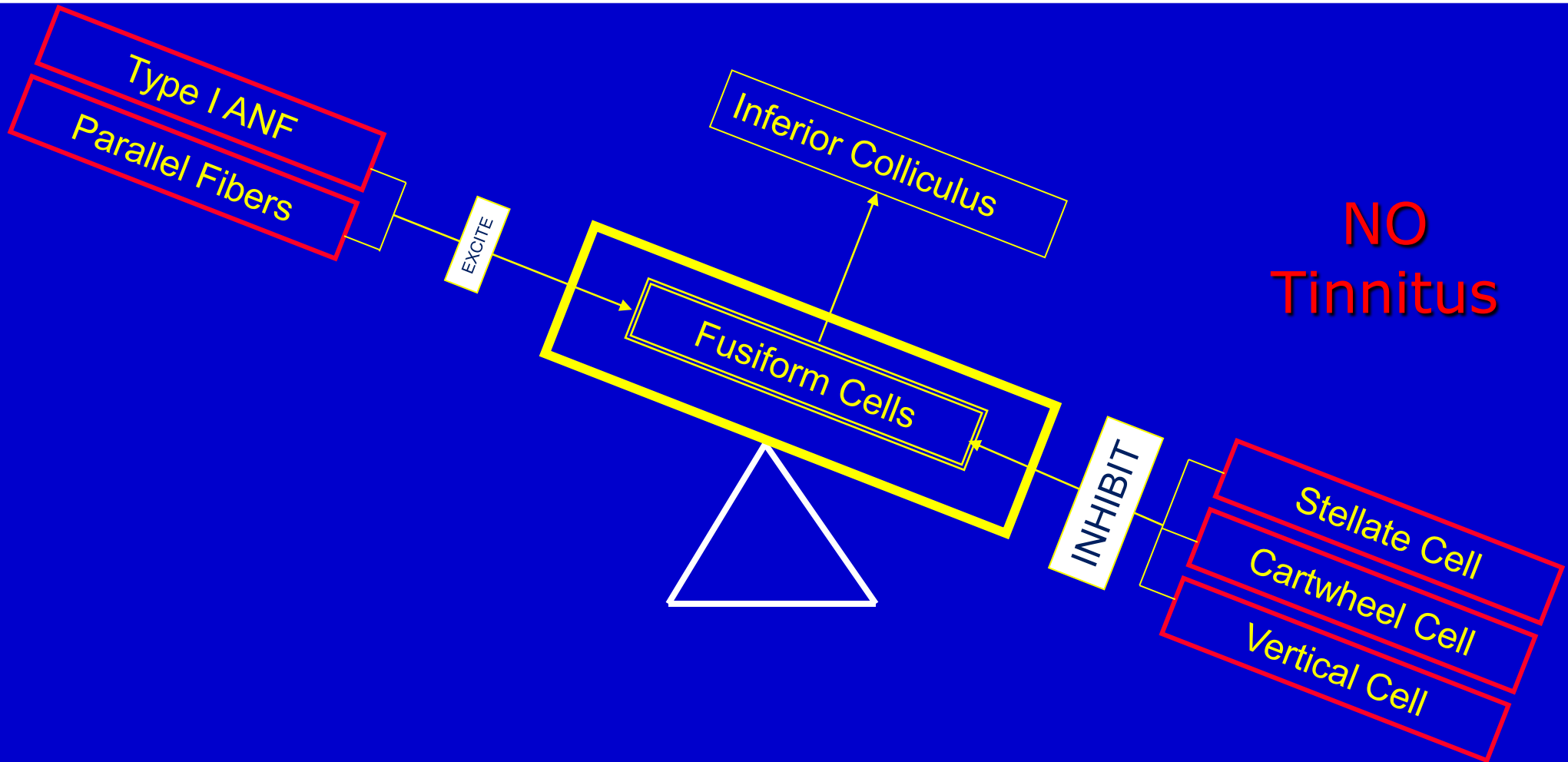


If tinnitus is due to elevated fusiform cell activity, then whether or not someone has tinnitus from a hearing loss will depend upon the relative interplay in changes in the degree of excitation and inhibition upon the fusiform cell.

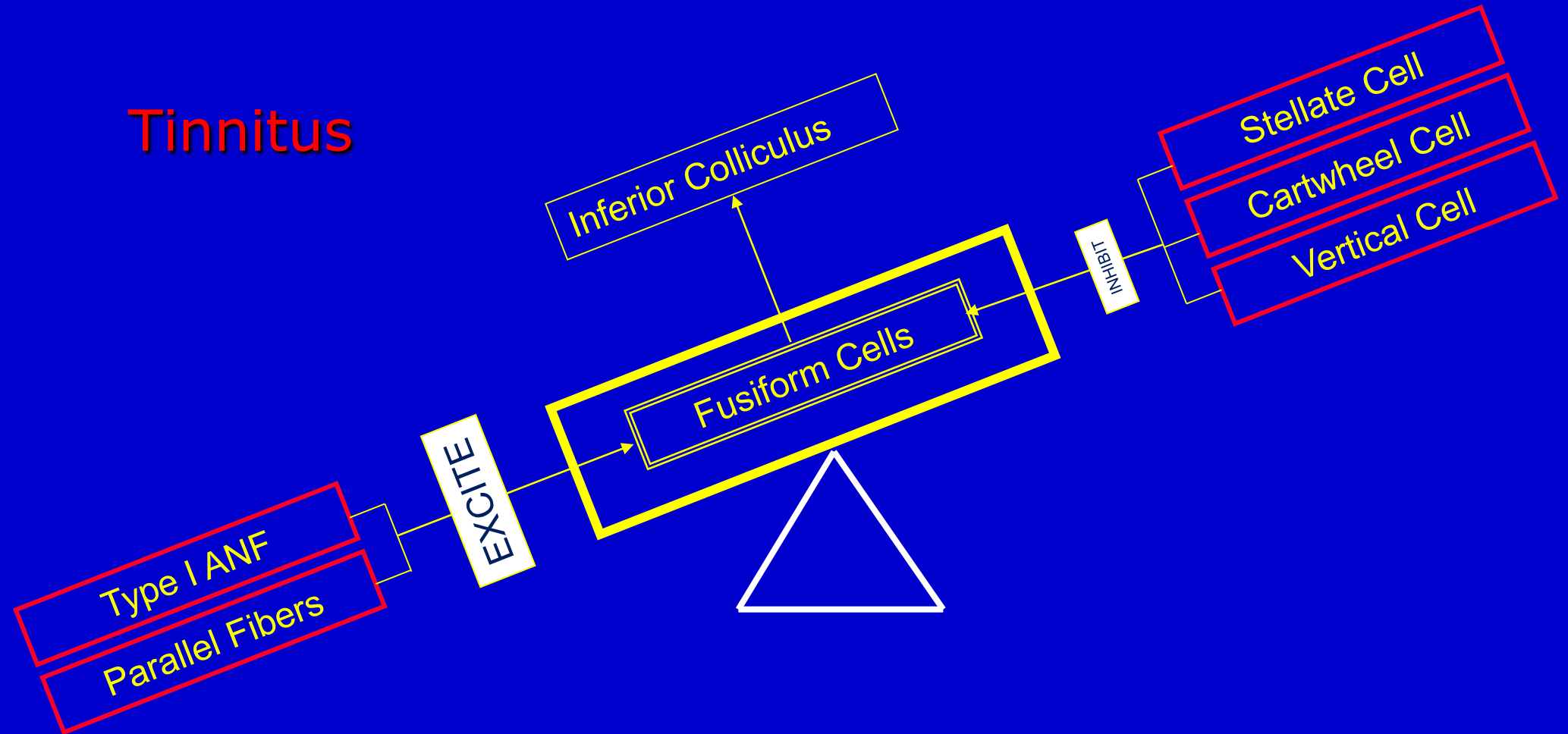
In general the prevalence of tinnitus is directly related to the degree of hearing loss. But for any degree of hearing loss, some people will have tinnitus and others will not. The extreme cases are total hearing loss including transection of the cochlear nerve. In such people about 1 in 4 will NOT develop tinnitus.

On the assumption that hearing loss is associated with decreased inputs from either Type I or Type II ANFs or both, then whether or not tinnitus develops from hearing loss will depend upon the relative changes in the degree of excitation and inhibition that impacts the fusiform cell.

If excitation is lost more than inhibition, then tinnitus will not result from the hearing loss.

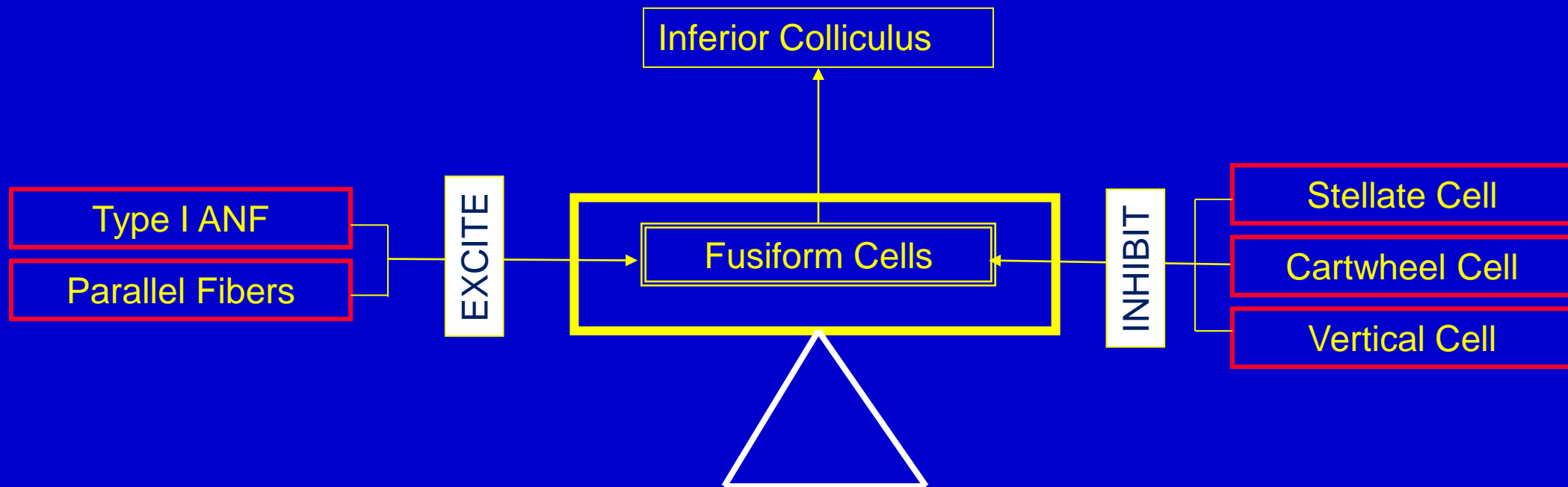


If the opposite occurs, inhibition is lost more than excitation, then tinnitus will develop.



This formulation can then account for why, for any degree of hearing loss, some DO and some DO NOT develop tinnitus. This formulation would apply as well to the extreme case of total hearing loss, such as cochlear nerve transection

Tinnitus or NO Tinnitus: Competing for the FUSIFORM CELL



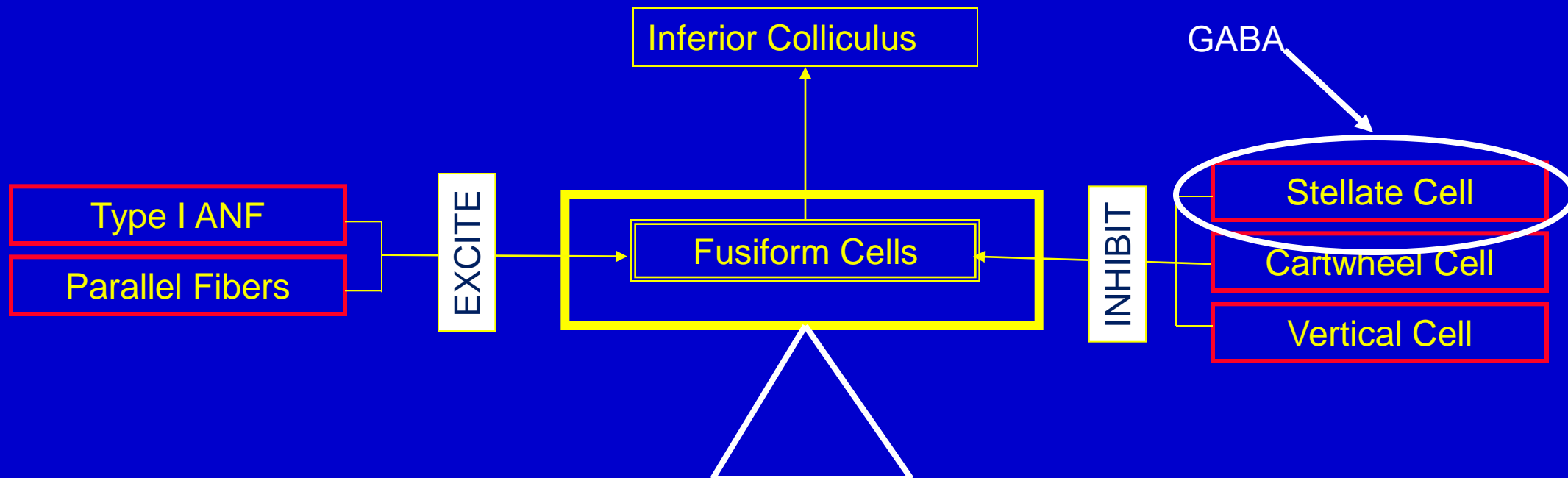
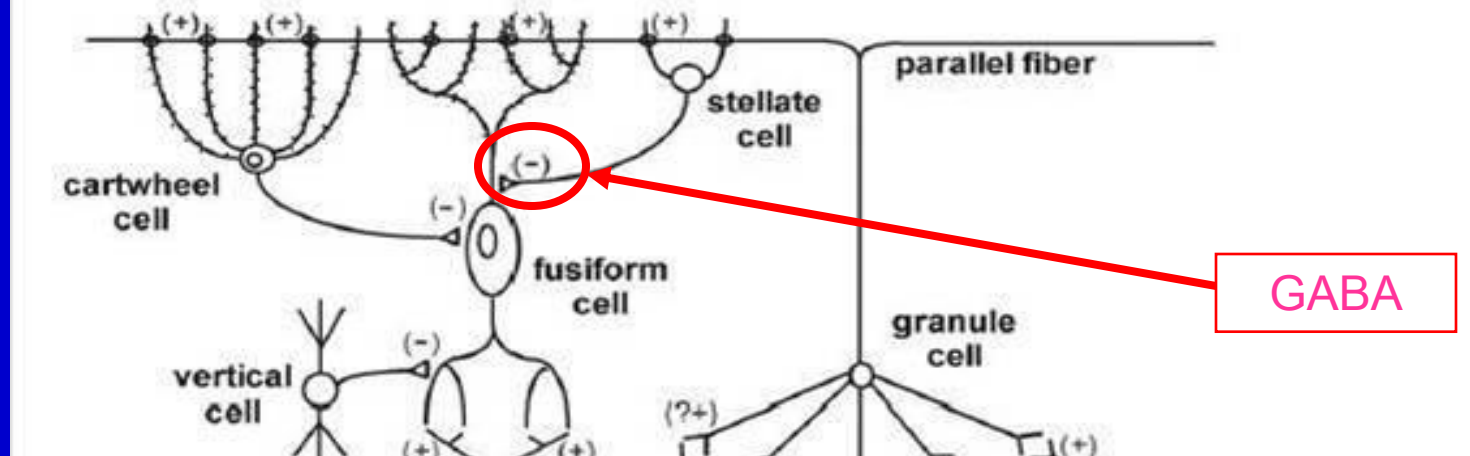
Corollary to this Formulation:

Things that promote inhibition (or decrease excitation) of the fusiform cell will quiet tinnitus.

This could explain why:

A. GABAergic drugs quiet tinnitus (human and animal studies).

Inhibition of the fusiform cell is mediated in part by GABA



In humans three well-designed studies have shown that the GABA potentiators, benzodiazepines, quiet tinnitus in about 75% of people

(a) Alprazolam (Xanax) 76% randomized, double-blind, placebo controlled [*Johnson et al. 1993*]

(b) Bromazepam (Lexotan) 78% double-blind, placebo-controlled study

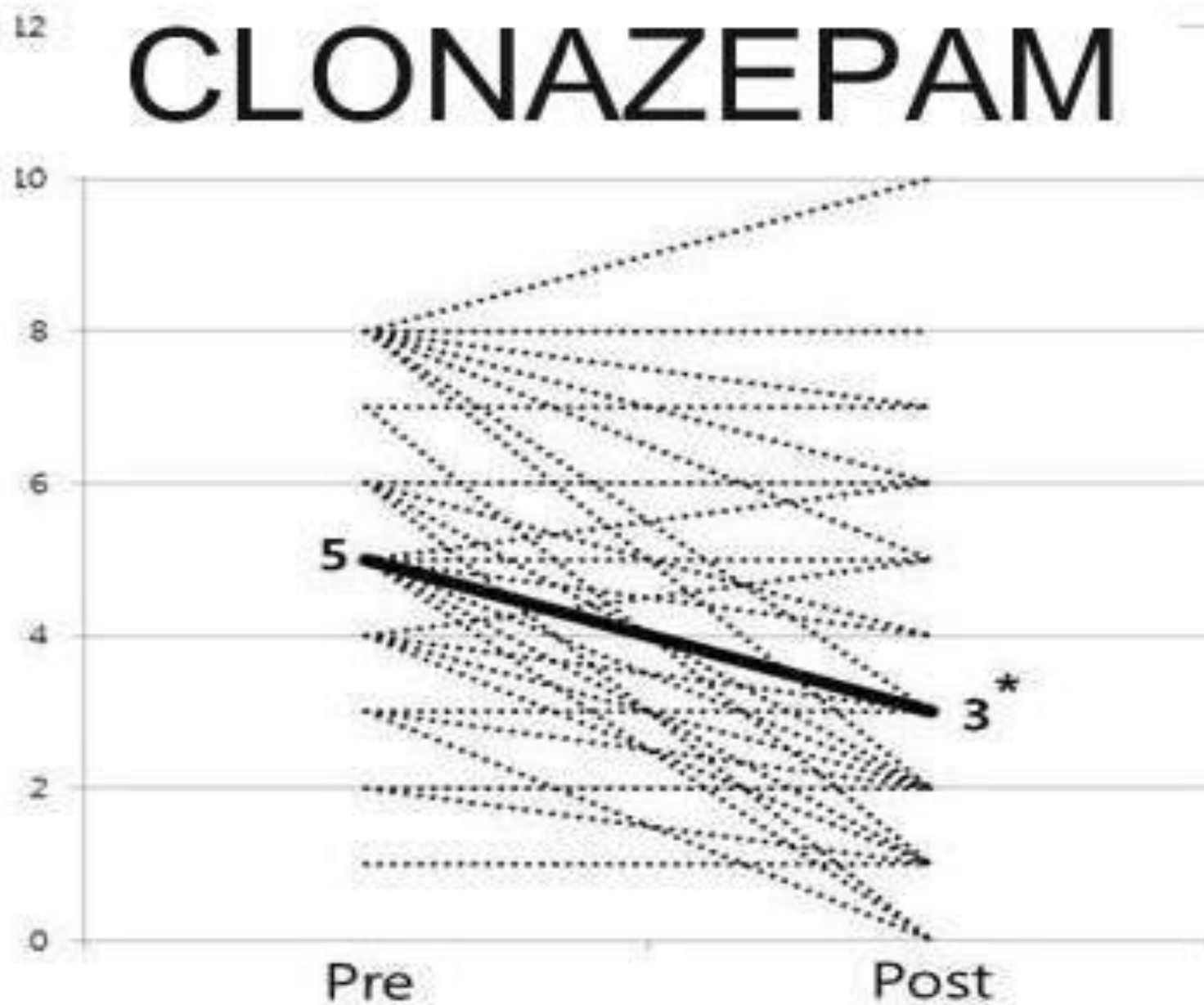
(c) Clonazepam (Klonopin) 74% cross-over study with Ginko Biloba [*Nam et al. submitted*]

Two other GABA potentiating drugs, Primidone (Mysoline) 86% and EtOH have also been shown to quiet tinnitus in humans (but in less rigorous studies).

In animals vigabatrin, a GABA potentiator, reversibly abolishes behavioral evidence of tinnitus.

CLONAZEPAM

Loudness (VAS)

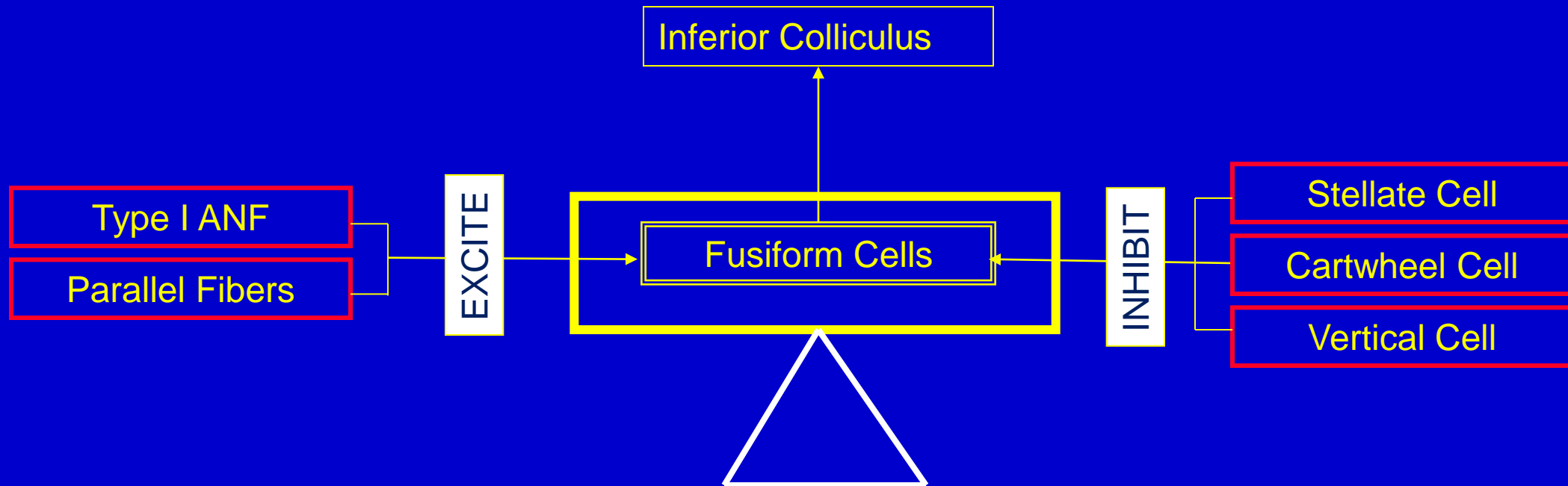


B. Electrical stimulation of the cochlear nerve quiets tinnitus (human studies).

Possibly from activation of inhibition (vertical, cartwheel, or stellate cells) or deactivation of fusiform cell excitation (Type I ANF or parallel fibers)

Multiple studies have shown such an effect.

Tinnitus or NO Tinnitus:
Competing for the FUSIFORM CELL



CONCLUSION: This elaboration of the DCN model provides a framework for developing improved tinnitus treatments from blast injuries such as:

- (A) Modifying cochlear nerve electrical stimulation to optimize vertical, stellate and cartwheel cell activation, while minimizing Type I auditory nerve and parallel fiber activation of the fusiform cell,
- (B) Modifying somatosensory inputs to the granule cell domain to optimize stellate and cartwheel cell activation while minimizing activation of the fusiform cell by the parallel fibers
- (C) Developing more medications, like the benzodiazepines, that will either promote fusiform cell inhibition or diminish excitation.

- **Collaborators**
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